

Application No.: 09/485,245

**RESPONSE UNDER 37 C.F.R. 1.16
Expedited Procedure
Examining Group 1645**

Docket No.: 28911/36128

REMARKS/ARGUMENTS**I. Preliminary Remarks**

In an effort to expedite allowance of its claims, but without prejudice to pursuing such claims in a continuing application, Applicant has cancelled its composition claims 1 and 3-6 and submits new claims 7-10 which recite the inventive subject matter of the application as a method. While Applicant maintains that its composition claims derive their patentability from the unexpected properties Applicant acknowledges the Examiner's concerns and submits that the novelty and unobviousness of its invention will be better appreciated when presented as method claims.

Accordingly, claims 7-10 present the invention as a method for preventing the self-annealing among random mixtures of oligonucleotides comprising the steps of forming a solution of a random mixture oligonucleotides which are 6-mers to 8-mers and drying the solution. This invention provides an improvement in random priming methods where random sequence oligonucleotides are used to prime DNA synthesis on denatured template DNA at numerous sites along its length.

There had been a trend toward using longer primers in solution in order to provide more rapid priming. (Megaprime and Ready-To-Go kits) Nevertheless, Suganuma suggested that shorter primers might be desired for liquid primer solutions because of self-annealing properties of larger primers in solution. Dried primer kits were also known for use with 9-mer and higher primers. (Rediprime, EP 298,269 discloses 15-mers and 17-mers) These were not thought to be subject to the problem of Suganuma. Moreover, there still remained a bias preferring longer primers because of the belief that such longer primers would provide more rapid priming than shorter primers.

The present invention relates to the discovery that there is a self-annealing problem with dried primers and that the solution to that problem is the use of shorter dried primers. Accordingly, the invention provides a method for preventing self-annealing that occurs among random oligonucleotides used in dried predisposed labeling kits and relates to

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the recognition that the problem is specific to 9-mers (and longer oligonucleotides) used in dried kits and does not represent a problem with shorter dried primers.

II. The Outstanding Rejections

Claims 1 and 3-5 are rejected under 35 U.S.C. 103(a) over Godiska et al., U.S. 5,759,804 in view of Shen et al., EP 0 726 310 A1.

Claim 6 stands rejected under 35 U.S.C. 103(a) over Godiska et al., U.S. 5,759,804 in view of Shen et al., EP 0 726 310 A1 in further view of Hoeltke et al., U.S. 5,814,502.

III. The Rejections Under 35 U.S.C. 103(a) Should be Withdrawn and Not Repeated against New Claims 7-10.

The obviousness rejections under 35 U.S.C. §103(a) should be withdrawn and not repeated against new claims 7-10 because the art fails to teach the desirability of short primers (6-8 mers) in a dried primer system or that 6-mers to 8-mers would behave differently with respect to self-priming activity and labeling intensity than do 9-mers.

More specifically, there is nothing in Godiska that teaches (1) that the selection of 6-mers to 8-mers constitutes a critical range (see the application examples) and (2) that short primers (6-8 mers) would be desirable in a dried primer system. While Godiska discloses a random mixture of 6-mers and other ingredients the Examiner acknowledges that Godiska does not teach a labeling composition in a dry state. Moreover, there is nothing in Godiska that teaches that the selection of 6-mers to 8-mers is important in either the liquid or freeze dried state to reduce self-annealing. In fact, self annealing is not mentioned at all!

In addition, Shen, which discloses 48-mer and 22-mer primers (Example 1 and SEQ ID NOS 1 and 2) fails to suggest that dried primers should be shortened or alternatively any reason why the primers of Godiska should be dried. This is because the prior art generally taught that longer primers were preferred because longer primers have higher melting temperatures and are thus more specific.

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Moreover, Shen acknowledges that "whether a particular composition will function to preserve biological activity for a particular biologically active material is not a priori predictable" (page 4, lines 36-37) and only discloses freeze-drying as an "option" (pg 5, lines 14-15) and In addition, Shen fails to provide any reason why the primers of Godiska should be dried given the fact that shorter primers were thought to be inherently more stable and there was no reason to believe that the shorter Godiska primers would benefit from being in freeze-dried kits.

For these reasons, the rejections under 35 U.S.C. §103 (a) should properly be withdrawn and not repeated against method claims 7-10. Should the Examiner have any questions or comments of form on substance, she is encouraged to contact the undersigned attorney.

CONCLUSION

In view of the foregoing remarks, claims 7-10 are believed to be in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested. Should the Examiner have any concerns of either form or substance she is encouraged to contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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